HED DOC. NO. 013987

February 10, 2000

MEMORANDUM

SUBJECT: ***DISULFOTON*** **-** Report of the FQPA Safety Factor Committee.

The FQPA safety factor recommendation in this report supercedes that previously reported for disulfoton in the FQPA SAFETY FACTOR RECOMMENDATIONS FOR THE ORGANOPHOSPHATES dated August 6, 1998.

FROM: Brenda Tarplee, Executive Secretary
FQPA Safety Factor Committee
Health Effects Division (7509C)

THROUGH: Ed Zager, Chairman
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PC Code: 032501

The FQPA Safety Factor Committee met on January 24, 2000 to re-evaluate the hazard and exposure data for disulfoton, and recommended that the FQPA Safety Factor (as required by Food Quality Protection Act of August 3, 1996) be removed (1x) in assessing the risk posed by this chemical. The FQPA safety factor recommendation in this report supercedes that previously reported for disulfoton in the *FQPA SAFETY FACTOR RECOMMENDATIONS FOR THE ORGANOPHOSPHATES* dated August 6, 1998.

I. HAZARD ASSESSMENT

A. Adequacy of Toxicology Database

On January 19, 2000, the HIARC reviewed the submitted acute delayed neurotoxicity study with disulfoton in the hen which was previously identified as data gap. The HIARC determined that this study is acceptable and therefore, toxicology database is now adequate according to the standard Subdivision F and/or OPPTS Series 870 Guideline requirements for a food-use chemical.

B. Evaluation of Neurotoxicity

The repeat acute delayed neurotoxicity study in hens (required by HIARC during the Hazard Assessment of the Organophosphates; May 12-14, 1998) has been received and reviewed, and found to be negative for organophosphate induced delayed neuropathy (OPIDP).

There are also acute and subchronic neurotoxicity studies with disulfoton in rats. The acute study shows neurotoxicity in the form of tremors and muscle twitching and decreased motor activity, but no neuropathology (MRID No. 42755801). The subchronic study shows similar neurotoxicity and nominal increased incidence of neuropathy in the form of nerve fiber degeneration in the optic nerve and thoracic spinal cord at the highest dose tested (MRID No. 42977401). On January 19, 2000, the HIARC concluded that the differences in the effects observed between the high dose animals and control animals in the subchronic neurotoxicity study in rats, were not sufficiently great to indicate that a treatment-related effect had occurred.

C. Developmental Toxicity

In a prenatal developmental toxicity study in rats, developmental toxicity occurred only in the presence of maternal toxicity (MRID No. 00129458).

In a prenatal developmental toxicity study in rabbits, there was no evidence of developmental toxicity even at the highest dose tested (MRID No. 00147886).

D. Reproductive Toxicity

In a two-generation reproduction study rats, the effects in pups were caused by maternal toxicity and not the direct toxicity of disulfoton on pups (MRID No. 44440801).

E. Determination of Developmental Neurotoxicity Study

On January 19, 2000, the HIARC concluded that although a developmental neurotoxicity study with disulfoton in rats has been required as part of the Data Call-In for select organophosphates, this requirement was not, however, 'triggered' by a special concern

for the developing fetuses or young which are generally used for requiring a DNT study and an FQPA safety factor (e.g.: neuropathy in adult animals; CNS malformations following prenatal exposure; brain weight or sexual maturation changes in offspring; and/or functional changes in offspring).

F. Determination of Susceptibility

Prenatal developmental toxicity studies in rats and rabbits provided no indication of increased susceptibility of rat or rabbit fetuses to *in utero* exposure to disulfoton. There was no indication of increased susceptibility in the offspring as compared to parental animals in the two generation reproduction study. In these studies, effects in the fetuses/offspring were observed only at or above treatment levels which resulted in evidence of maternal/parental toxicity.

II. EXPOSURE ASSESSMENTS

A. Dietary (Food) Exposure Considerations

(*Correspondence:* D.G. Anderson to E. Zager dated January 24, 2000)

Disulfoton is a systemic insecticide/acaricide. Permanent tolerances have been established for the combined residues of disulfoton and its chloinesterase-inhibiting metabolites calculated as demeton in/on many raw agricultural commodities at levels ranging from 0.1 ppm (peppers and soybeans) to 12 ppm (alfalfa and clover hay) [40 CFR §180.183]. There are Codex Maximum Residue Limits (MRLs) established for many commodities.

Disulfoton is used on many foods which are considered to be highly consumed by infants and children, including beans, corn, peas, potatoes, rice, oats, soybeans, and wheat (1993 NAS report, Pesticides in the Diets of Infants and Children).

Residue data sources available for disulfoton include: field trial data; Pesticide Data Program (PDP) monitoring data; FDA surveillance data; and FDA Total Diet Survey data. Additionally, disulfoton (analyzed as disulfoton o-analog sulfone) is included in the Organophosphate Market Basket Survey sponsored by the Market Basket Survey Task Force (OPMBS-01; NSI SURVEY 98-02). Information on percent of crop treated (%CT) is also available from the Biological and Economic Analysis Division (BEAD) for this pesticide.

PDP monitoring data (1996 and 1997) found no quantifiable residues of disulfoton or disulfoton sulfone in a total of 11,106 fruit and vegetable samples analyzed including apples, apple juice, carrots, grapes, green beans, oranges, orange juice, peaches, pears, spinach, sweet corn, sweet peas, sweet potatoes, tomatoes, and winter squash (LOD $\leq$0.043 ppm); a total of 1011 milk samples screened (LOD $\leq$0.002 ppm); and in a total of 158 soybean samples screened (LOD $\leq$0.003 ppm). PDP also reported no quantifiable residues of demeton-S in a total of 870 fruit and vegetable samples tested (apples, oranges, orange juice, peaches, and spinach - LOD $\leq$0.043 ppm); and a total of 963 wheat

samples tested (LOD = 0.006 ppm). Twelve detections of demeton-S sulfone were reported by PDP: 11 in green beans (maximum value = 0.010 ppm); and 1 in spinach at 0.013 ppm. There were no reported detections of demeton-S sulfone in a total of 202 milk samples screened (LOD $\leq$0.003).

The HED Dietary Exposure Evaluation Model (DEEM) is used to assess the risk from acute and chronic dietary exposure to residues of disulfoton in food. These analyses are highly refined using anticipated residues from monitoring and field trial data and the available %CT information.

B. Dietary (Drinking Water) Exposure Considerations
(*Correspondence:* D.G. Anderson to E. Zager dated January 24, 2000)

The environmental fate database for disulfoton is incomplete with regard to the degradates of disulfoton. The available fate data indicate that the parent, disulfoton, has low to moderated persistence in the environment with the sulfoxides and sulfone degradates being more mobile and stable than the parent. EFED concludes that there is potential for disulfoton to enter the surface and ground water, especially at the maximum label use rates.

Limited monitoring data were used to estimate ground water concentrations. These data were used since detection were noted in about one-half of the wells sampled in Virginia and Wisconsin at 4.4 μg/L (range 0 to 100 μg/L). These detections were noted in sandy soils, which are considered the most vulnerable soils. No detections were noted in over 2400 well samples from 11 states.

The drinking water assessment is based on models and limited monitoring data from wells in Virginia and Wisconsin. The estimated environmental concentrations (EECs) were calculated using the available monitoring data in the GENEEC and PRZM/EXAMS models for surface water, and the SCI-GROW (Tier 1) model for ground water.

C. Non-Occupational (Residential) Exposure Considerations
(*Correspondence:* D.G. Anderson to E. Zager dated January 24, 2000)

Residential (non-occupational) uses of disulfoton include treatment to roses; flower and vegetable gardens; shrubs and small trees; and potted plants. Disulfoton is also use in "insecticidal spikes" that are placed in the soil around plants (and in plant pots). Post application exposure to infants and children could occur with these uses.

No chemical-specific data for disulfoton are available to assess exposure during or after outdoor residential application. Therefore, the DRAFT Standard Operating Procedures (SOPs) for Residential Exposure Assessments will be used to estimate the potential exposure using surrogate data. The DRAFT SOPs normally rely on one or more upper-percentile assumptions and are intended to represent Tier 1 screening assessments.

III. SAFETY FACTOR RECOMMENDATION AND RATIONALE

A. Recommendation of the Factor

The Committee recommended that the FQPA safety factor for protection of infants and children (as required by FQPA) be **removed (1x).**

B. Rationale for Removing the FQPA Safety Factor

The Committee concluded that the safety factor could be removed because:

1. The acute delayed neurotoxicity study with disulfoton in the hen which was previously identified as data gap has been received, reviewed, and found to be negative;

2. The standard toxicity data provided no indication of quantitative or qualitative increased susceptibility of rats or rabbits to *in utero* and/or postnatal exposure;

3. the requirement of a developmental neurotoxicity study is not based on the criteria reflecting some special concern for the developing fetuses or young which are generally used for requiring a DNT study and an FQPA safety factor (e.g.: neuropathy in adult animals; CNS malformations following prenatal exposure; brain weight or sexual maturation changes in offspring; and/or functional changes in offspring)[1] and therefore does not warrant an FQPA safety factor; and

4. The exposure assessments will not underestimate the potential dietary (food and water) and non-dietary (residential) exposures for infants and children from the use of disulfoton.

[1]This is an interim step towards accordance with the proposed 'OPP POLICY ON DETERMINATION OF THE APPROPRIATE FQPA SAFETY FACTOR(S) FOR USE IN THE TOLERANCE-SETTING PROCESS' which was presented to the FIFRA SAP meeting in May, 1999 and placed in the Docket for Public Comment (64FR37001; 7/8/99; Docket No. 37001).